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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,934	03/12/2004	Mark Kelly	066692-0097	6830

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MCDERMOTT, WILL & EMERY  
11682 EL CAMINO REAL  
SUITE 400  
SAN DIEGO, CA 92130-2047

EXAMINER
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STEELE, AMBER D

ART UNIT	PAPER NUMBER
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1639

MAIL DATE	DELIVERY MODE
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02/12/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/799,934	<b>Applicant(s)</b> KELLY ET AL.	
	<b>Examiner</b> AMBER D. STEELE	<b>Art Unit</b> 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on December 21, 2007 and November 21, 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-90 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/21/07</u> .  | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-47,52,53,55,56,58,60-65,70,71,73,74,76,77 and 81-90.

## **DETAILED ACTION**

### ***Status of the Claims***

1. The amendment to the claims received on February 28, 2007 added status identifiers only.

The amendment to the claims received on November 21, 2008 amended claims 48, 50-51, 66, and 68-69.

Claims 1-90 are currently pending.

Claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 are currently under consideration.

### ***Election/Restrictions***

2. Applicants elected, without traverse, Groups VI-VII (i.e. rejoined Groups VI-VII; no traversal of restriction between other groups) in the reply filed on February 28, 2007. Claims 1-47, 63-65, and 82-90 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

3. Applicants elected, without traverse, a singular antenna moiety as the species of antenna moiety, competitive binding as the species of identification, and 2D NOESY as the species of NOESY in the reply filed on February 28, 2007. Claims 52-53, 55-56, 58, 70-71, 73-74, 76-77, and 81 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim.

### ***Priority***

4. The present application claims the benefit of U.S. provisional application 60/455,610 filed March 13, 2003.

***Information Disclosure Statement***

5. The information disclosure statement (IDS) submitted on December 27, 2007 is being considered by the examiner.

***Specification***

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

***Sequence Compliance***

7. The present application is currently in compliance with the sequence rules in view of the responses received on April 14, 2008.

***Withdrawn Objection***

8. The objection to claims 48-51, 54, 57, and 59-61 is withdrawn in view of the claim amendments received on November 21, 2008.

***Invention as claimed***

9. A method for obtaining a "focused" library of candidate binding compounds for a protein family, wherein the members of the protein family bind a common ligand, comprising the steps of: (a) providing a ligand-probe having an antenna moiety, wherein the ligand-probe binds to the common ligand binding site of a protein, wherein the protein is a member of the protein family; (b/c) providing a sample or plurality thereof comprising the protein, the ligand-probe, and a second ligand under conditions wherein the ligand-probe, the second ligand, and the protein form a bound complex; (c/d) detecting/assaying a subset of magnetization transfer signals (from the second ligands) between the antenna moiety of the ligand-probe and the second ligand in the

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bound complex, wherein said signals are obtained from an isotope-edited NOESY spectrum of said sample, thereby determining that the antenna moiety and the second ligand are proximal in the bound complex; and (d/e) obtaining a population of candidate binding compounds comprising the ligand-probe or a fragment thereof that binds to the common ligand binding site of said protein covalently linked to one of a plurality of homologs of said second ligand whereby the population contains binding compounds that bind to members of the protein family and variations thereof.

#### **Withdrawn Rejections**

10. The rejections of claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention regarding “second ligand homologs”, “homologs”, “fragments”, “homologs”, “isotope-edited”, and “linkage” are withdrawn in view of the claim amendments received on November 21, 2008.

#### **Maintained Rejections**

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections - 35 USC § 102***

12. Claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 are rejected under 35 U.S.C. 102(b) as being anticipated by Sem U.S. Patent 6,333,149 issued December 25, 2001.

For present claims 48 and 66, Sem teaches methods for rapidly identifying drug candidates that bind an enzyme at both a common ligand site and a specificity ligand site wherein the drug candidates are screened from a focused combinatorial library comprising (a)

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providing a CL or common ligand attached to an isotope or antenna moiety, (b) providing a sample or a library of samples comprising an enzyme or protein, CL/isotope, and a mimic and/or SL (i.e. second ligand and/or homolog) that can form a binary and/or ternary complex, (c) utilizing NMR and thus the magnetization of NMR including NOESY to obtain signals and spectrum to determine the proximity of the CL, SL, mimic, and/or enzyme, (d) obtaining a library of mimics covalently linked to CL (please refer to the entire specification particularly abstract; Figures 1A-7B; columns 1-13; Examples; claims).

For present claims 49 and 67, Sem teaches CL or common ligand including NADH or NADD (i.e. ligand-probe) attached to an isotope or with a hydrogen to deuterium substitution (i.e. antenna moiety; please refer to the entire specification particularly column 16, lines 51-65).

For present claims 50 and 68, Sem teaches obtaining a library of binary and/or ternary complexes including CL or common ligand linked to a mimic or second ligand homolog (please refer to the entire specification particularly Figures 1A, 1B, 2A, 2B, 3A, 3B, 3C, 4B, 5A, 5B, 5C, 5D; columns 7-8, 10-11, 16).

For present claims 51 and 69, Sem teaches potential linkages between the isotope or antenna moiety and the mimic or second ligand homolog (please refer to the entire specification particularly Figures; columns 7, 10).

For present claims 54 and 72, Sem teaches competitive binding (please refer to the entire specification particularly columns 7-8 particularly the paragraph spanning the columns; column 15, lines 30-49; column 17, lines 37-54).

For present claims 57 and 75, Sem teaches deuterium isotopes (please refer to the entire specification particularly column 3, lines 22-28; column 6, lines 66-67; column 7, lines 1-8; column 8, lines 20-44; columns 9-10, 16).

For present claims 59-60 and 78-79, Sem teaches identifying the atom of the isotope proximal to the atom of the mimic or SL/specificity ligand site and also determining the distance (i.e. second ligand; please refer to the entire specification particularly columns 7-11).

For present claims 61 and 80, Sem teaches 2D NOESY (please refer to the entire specification particularly column 3, lines 22-46; column 9).

### *Arguments and Response*

13. Applicants' arguments directed to the rejection under 35 USC 102 (b) as being anticipated by Sem for claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 were considered but are not persuasive for the following reasons.

Applicants contend that Sem provides no teaching of a method for obtaining a focused library of candidate binding compounds for a protein family as in Applicant's claimed methods.

Applicants' arguments are not convincing since the teachings of Sem anticipate the methods of the instant claims. Sem teaches methods for rapidly identifying drug candidates that bind an enzyme at both a common ligand site and a specificity ligand site wherein the drug candidates are screened from a focused combinatorial library comprising (a) providing a CL or common ligand attached to an isotope or antenna moiety, (b) providing a sample or a library of samples comprising an enzyme or protein, CL/isotope, and a mimic and/or SL (i.e. second ligand and/or homolog) that can form a binary and/or ternary complex, (c) utilizing NMR and thus the magnetization of NMR including NOESY to obtain signals and spectrum to determine the



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proximity of the CL, SL, mimic, and/or enzyme, (d) obtaining a library of mimics covalently linked to CL (please refer to the entire specification particularly abstract; Figures 1A-7B; columns 1-13; Examples; claims).

### ***Double Patenting***

14. Claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 6,333,149. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed method and the method of U.S. Patent 6,333,149 comprise identifying homologs/mimics of proteins/enzymes.

For present claims 48 and 66, U.S. Patent 6,333,149 claims methods comprising (a) providing a CL (i.e. ligand-probe) with an atom (i.e. antenna) and an enzyme (i.e. protein), (b) providing a CL mimic and/or a SL (i.e. second ligand), (c) performing NMR (i.e. magnetization transfer signals between atoms to determine proximity) including NOESY, (d) identifying the CL mimic thus obtaining candidate binding compounds (please refer to claims 1-4 and 29).

For present claims 49 and 67, U.S. Patent 6,333,149 claims an atom of the CL (i.e. antenna attached to the common ligand; please refer to claims 1-4, 20, 22).

For present claims 50 and 68, U.S. Patent 6,333,149 claims CL linked or in proximity to SL or CL mimic (i.e. second ligand; please refer to claims 1-4, 14, 21).

For present claims 51 and 69, U.S. Patent 6,333,149 claims proximity (i.e. linkage) between CL atoms and CL mimic atoms or SL atoms (please refer to claims 1-4, 14, 21).

For present claims 54 and 72, U.S. Patent 6,333,149 claims competitive binding (please refer to claims 1-4).

For present claims 57 and 75, U.S. Patent 6,333,149 claims deuterium (please refer to claim 31).

For present claims 59-60 and 78-79, U.S. Patent 6,333,149 claims identifying atoms and distance via Angstroms (please refer to claims 1-4 and 32-33).

For present claims 61 and 80, U.S. Patent 6,333,149 claims two dimensional NOESY wherein the two dimensional is produced via combining two one dimensional spectrums (please refer to claims 1-4 and 29).

### *Arguments and Response*

15. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over U.S. Patent 6,333,149 for claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 were considered but are not persuasive for the following reasons.

Applicants request that the rejection be held in abeyance.

While a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the rejection above will not be held in abeyance. See MPEP § 714.02.

16. Claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-62 of U.S. Patent No. 6,620,589. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed method and the method of U.S. Patent 6,620,589 comprise identifying homologs/mimics of proteins/enzymes.

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For present claims 48 and 66, U.S. Patent 6,620,589 claims methods comprising (a) providing a CL (i.e. ligand-probe) with an atom (i.e. antenna) and an enzyme (i.e. protein), (b) providing a CL mimic and/or a SL (i.e. second ligand), (c) performing NMR (i.e. magnetization transfer signals between atoms to determine proximity) including NOESY, (d) identifying the CL mimic thus obtaining candidate binding compounds (please refer to claims 1-2, 8, 44, 47, 55-56, 59-62).

For present claims 49 and 67, U.S. Patent 6,620,589 claims an atom of the CL (i.e. antenna attached to the common ligand; please refer to claims 1-5, 8-12, 44, 55-56, 59-62).

For present claims 50 and 68, U.S. Patent 6,620,589 claims CL linked or in proximity to SL or CL mimic (i.e. second ligand; please refer to claims 1-5, 8-12, 55-56, 59-62).

For present claims 51 and 69, U.S. Patent 6,620,589 claims proximity (i.e. linkage) between CL atoms and CL mimic atoms or SL atoms (please refer to claims 1-5, 8-12, 55-56, 59-62).

For present claims 54 and 72, U.S. Patent 6,620,589 claims competitive binding (please refer to claims 1-2, 8, 55-56, 59-62).

For present claims 57 and 75, U.S. Patent 6,620,589 claims deuterium (please refer to claims 49, 51-52, 57).

For present claims 59-60 and 78-79, U.S. Patent 6,620,589 claims identifying atoms and distance via Angstroms (please refer to claims 1-2, 8, 44, 53-56, 59-62).

For present claims 61 and 80, U.S. Patent 6,620,589 claims two dimensional NOESY wherein the two dimensional is produced via combining two one dimensional spectrums (please refer to claims 1-2, 8, 44, 47, 55-56, 59-62).

*Arguments and Response*

17. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over U.S. Patent 6,620,589 for claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 were considered but are not persuasive for the following reasons.

Applicants request that the rejection be held in abeyance.

While a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the rejection above will not be held in abeyance. See MPEP § 714.02.

18. Claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-160 of U.S. Patent No. 6,797,460. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed method and the method of U.S. Patent 6,797,460 comprise identifying homologs/mimics of proteins/enzymes.

For present claims 48 and 66, U.S. Patent 6,797,460 claims methods comprising (a) providing a CL (i.e. ligand-probe) with an atom (i.e. antenna) and an enzyme (i.e. protein), (b) providing a CL mimic and/or a SL (i.e. second ligand), (c) performing NMR (i.e. magnetization transfer signals between atoms to determine proximity) including NOESY, (d) identifying the CL mimic thus obtaining candidate binding compounds (please refer to claims 1, 33, 36, 41, 73, 76, 81, 113, 116, 121, 153, 156).

For present claims 49 and 67, U.S. Patent 6,797,460 claims an atom of the CL (i.e. antenna attached to the common ligand; please refer to claims 1, 33, 36, 41, 73, 76, 81, 113, 116, 121, 153, 156).

For present claims 50 and 68, U.S. Patent 6,797,460 claims CL linked or in proximity to SL or CL mimic (i.e. second ligand; please refer to claims 1, 33, 36, 41, 73, 76, 81, 113, 116, 121, 146-148, 153, 156).

For present claims 51 and 69, U.S. Patent 6,797,460 claims proximity (i.e. linkage) between CL atoms and CL mimic atoms or SL atoms (please refer to claims 1, 33, 36, 41, 73, 76, 81, 113, 116, 121, 146-148, 153, 156).

For present claims 54 and 72, U.S. Patent 6,797,460 claims competitive binding (please refer to claims 1, 33, 36, 41, 73, 76, 81, 113, 116, 121, 153, 156).

For present claims 57 and 75, U.S. Patent 6,797,460 claims deuterium (please refer to claims 38, 78).

For present claims 59-60 and 78-79, U.S. Patent 6,797,460 claims identifying atoms and distance via Angstroms (please refer to claims 1, 33, 36, 39-41, 73, 76, 79-81, 113, 116, 119-121, 153, 156, 159-160).

For present claims 61 and 80, U.S. Patent 6,797,460 claims two dimensional NOESY wherein the two dimensional is produced via combining two one dimensional spectrums (please refer to claims 33, 35-36, 73, 76, 113, 116, 153, 156).

### ***Arguments and Response***

19. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over U.S. Patent 6,797,460 for claims

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48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 were considered but are not persuasive for the following reasons.

Applicants request that the rejection be held in abeyance.

While a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the rejection above will not be held in abeyance. See MPEP § 714.02.

20. Claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-42 of U.S. Patent 7,252,931 (previously copending Application No. 10/884,181). Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed method and the method of U.S. Patent 7,252,931 comprise identifying homologs/mimics of proteins/enzymes.

For present claims 48 and 66, U.S. Patent 7,252,931 claims methods comprising (a) providing a CL (i.e. ligand-probe) with an atom (i.e. antenna) and an enzyme (i.e. protein), (b) providing a CL mimic and/or a SL (i.e. second ligand), (c) performing NMR (i.e. magnetization transfer signals between atoms to determine proximity) including NOESY, (d) identifying the CL mimic thus obtaining candidate binding compounds (please refer to previous claims 59-61, 86-91, 93-96, 98-100).

For present claims 49 and 67, U.S. Patent 7,252,931 claims an atom of the CL (i.e. antenna attached to the common ligand; please refer to previous claims 59-61, 86-91, 93-96, 98-100).

For present claims 50 and 68, U.S. application 10/884,181 claims CL linked or in proximity to SL or CL mimic (i.e. second ligand; please refer to previous claims 59-61, 86-91, 93-96, 98-100).

For present claims 51 and 69, U.S. Patent 7,252,931 claims proximity (i.e. linkage) between CL atoms and CL mimic atoms or SL atoms (please refer to previous claims 59-61, 86-91, 93-96, 98-100).

For present claims 54 and 72, U.S. Patent 7,252,931 claims competitive binding (please refer to previous claims 59-61, 86-91, 93-96, 98-100).

For present claims 57 and 75, U.S. Patent 7,252,931 claims deuterium (please refer to previous claim 98).

For present claims 59-60 and 78-79, U.S. Patent 7,252,931 claims identifying atoms and distance via Angstroms (please refer to previous claims 98-100).

For present claims 61 and 80, Patent 7,252,931 claims two dimensional NOESY wherein the two dimensional may be produced via combining two one dimensional spectrums (please refer to previous claims 59-61, 86-91, 93-96, 98-100).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Arguments and Response***

21. Applicants' arguments directed to the rejection on the provisional ground of nonstatutory obviousness-type double patenting as being unpatentable over U.S. Patent 7,252,931 for claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 were considered but are not persuasive for the following reasons.

Applicants request that the rejection be held in abeyance.

While a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the rejection above will not be held in abeyance. See MPEP § 714.02.

#### ***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/  
Patent Examiner, Art Unit 1639

February 9, 2009



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